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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,432	09/19/2003	Charles E. Hart	00-12D1	5728

10117 7590 01/25/2008

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

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01/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,432	HART ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9,11 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9,11 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's response filed on 09 November 2007 is acknowledged and entered.

Currently, claims 2-9, 11 and 22-25 are pending and under consideration.

Declaration

The prior art rejection of claims 2-5, 7-9, 11, 22, 23 and 25 rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al. (US6,455,283 B1), and the prior rejection of claims 6 and 24 under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al. (US6,455,283 B1), and further in view of Bentz et al. (EP 0 512 844 A1), set forth in the last Office actions are maintained.

The declaration under 37 CFR 1.132 filed on 09 November 2007 is insufficient to overcome the above mentioned prior rejections set forth in the last Office action because: the declaration is largely opinion/argument only, and presents no further supporting evidence. Applicants opinion and argument have been fully considered, but, they are not persuasive for the reasons below.

At pages 3-4 (items 11-14) of the declaration, Applicants argue that PDGF-C was unique as it has a two-domain structure including the growth factor domain (C-terminus) and an N-terminal CUB domain, and is active only upon cleavage of the CUB domain; that the polypeptide recited in the present invention corresponds to bioactive fragment of PDGF-C having the growth factor domain. Applicants further argue, on pages 4-6 of the declaration (items 15, 18, 19, 21 and 22), that Ferrara disclosed the same polypeptide (named "VEGF-E"), but the reference does not teach or suggest any particular active fragments of PDGF-C, nor that recited in the present claim 11 or 22; that Ferrara does not specifically teach or suggest a unique, two-domain structure for the polypeptide, in particular, Ferrara does not teach the approximate boundaries of the growth factor domain, nor does Ferrara disclose or suggest the proteolytic cleavage to release the active growth factor domain from the full-length protein; and that Ferrara does not teach or suggest the recited fragment or a method for using such a PDGF-C fragment to promote the

growth of bone, ligament, or cartilage, or to stimulate proliferation of osteoblasts or chondrocytes.

Applicants argument has been fully considered, but is not deemed persuasive because although Ferrara does not teach or suggest the recited fragment or the approximate boundaries of the growth factor domain, it is less relevant as mapping out a functional fragment or defining the structural-functional relationship of a newly discovered protein was both desirable and routine in the art at the time the present invention was filed, so long as the sequence and functional activity were known. In the instant case, what is important is the fact that the reference teaches the exact polypeptide sequence, active fragments (in general), and the functional activity of the polypeptide (stimulates cell proliferation, for example). Therefore, based on Ferrara's teaching, a person of ordinary skill in the art would readily be able to make the polypeptide fragments and test for functional activity following Ferrara's suggestions including making deletions at the N-terminus, and come up with fragments as that recited in the instant claims. Additionally, as addressed in the last Office Action, Ferrara also teaches the use of VEGF-E, among others, for the healing of bone fractures and cartilage damage or defect in humans or other animals.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal argument of nonobviousness fails to outweigh the evidence of obviousness.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-5, 7-9, 11, 22, 23 and 25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al., US6,455,283 B1 (provided by applicants), for the reasons of record set forth in the last Office Action mailed on 22 August 2007, at pages 2-4, and for the reasons above.

Applicants argument filed on 09 November 2007 has been fully considered, but is not deemed persuasive for the reasons below.

At pages 5-6 of the response, based on Dr. Jaspers Declaration, the applicant presents the similar argument as that Ferrara would not have been led to the fragment as recited in the present claims, and thus would not have been led to the claimed method; that, citing MPEP and case law, the legal standard under 35 U.S.C. § 103 is an objective one, to establish *the prima facie* case under § 103, the Examiner must show some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or combine reference teachings so as to achieve the specific combination as claimed by the applicant, and the suggestion or motivation to modify reference teachings must be found in the prior art and cannot be based on applicant's disclosure; and that a skilled artisan reading Ferrara would not have been specifically led to modify the polypeptide of Ferrara's SEQ ID NO:2 so as to achieve the protein recited in the instant claims. This argument is not persuasive for the following reasons. First, with respect to the legal standard under 35 U.S.C. § 103, the referred TSM analysis by applicants is, according to the recent Supreme Court decision (KSR International v. Teleflex), merely one of several criteria, which may be used for analyzing the obviousness 35 U.S.C. § 103. Further, although Ferrara does not teach the specific fragments of the polypeptide, as addressed above, determining the structural-functional relationship of a newly discovered polypeptide, and making functional fragments thereof are both desirable and routine in the art. Therefore, such determination for a known polypeptide and achieving

functional fragments thereof does not constitute novel inventive concept, given the fact that Ferrara has taught both the amino acid sequence and the functional property of the polypeptide.

At pages 6-8 of the response, applicant presents the similar argument as that in the Declaration that PDGF-C has a unique two-domain structure, PDGF-C is active only upon cleavage of the CUB domain from the growth factor domain, and partial deletion of the N-terminus is inadequate to generate an active fragment of PDGF-C; that a polypeptide chain as recited in the present claims 11 and 22 corresponds to a bioactive fragment of PDGF-C; and that although Ferrara teaches "active fragments" of VEGF-E (PDGF-C), the reference, however, does not teach or suggest any particular active fragments of PDGF-C, nor does provide any specific guidance as to which fragments would be active. This argument is not persuasive for the same reasons addressed above (under "*Declaration*").

At page 8 of the response, applicant further argue, similarly to that in the declaration, that previous to the effective filing date of the instant application, there was no disclosure or suggestion of a PDGF having a two-domain structure as observed for PDGF-C and which is secreted in mitogenieally inactive form; and that, therefore, as of the application's effective filing date, in view of Ferrara's lack of any teaching or suggestion regarding the two-domain structure of PDGF-C, the significance of this structure with respect to activation, and the absence in the art of other PDGFs having these characteristics, Ferrara would not have specifically suggested to a person of ordinary skill in the art to modify Ferrara's potypeptide of SEQ ID NO:2 to achieve a polypeptide as recited in claim 11 or 22 of the instant application. This argument is not persuasive because issues such as whether the polypeptide has a two-domain structure are irrelevant to the *claimed* invention. What is relevant is the claimed functional fragments, which, however, are obvious over the prior art given the fact that Ferrara has taught both the amino acid sequence and the functional property of the polypeptide, and indicated that active fragments are also desirable; and that it is routine in the art to determine the structural-functional relationship of a polypeptide, and to make functional fragments thereof.

Claims 6 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al., US6,455,283 B1, as applied to claims 2-5, 7-9, 11, 22, 23 and 25 above, and further in view of Bentz et al., EP 0 512 844 A1, for the reasons of record set forth in the last Office Action mailed on 22 August 2007, at pages 4-5, and for the reasons below.

At page 9 of the response, the applicant presents the similar argument as that in the declaration, as that Ferrara does not teach or suggest the use of a fragment of PDGF-C corresponding to the growth factor domain, as required by independent claims 11 and 22. Bentz does not cure these deficiencies of Ferrara. This argument is not persuasive for the same reasons above as the traverse is based on the same ground as that above.

Conclusion:

No claim is allowed.

Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Dong Jiang

Dong Jiang, Ph.D.
Patent Examiner
AU1646
1/12/08